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PATENT
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3/23/95
Date

Jean Hilenski
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

MICHAEL C. KIEFER and PHILIP J. BARR

Serial No.: 08/320,157 Group Art Unit: Unknown

Filing Date: 07 October 1994 Examiner: Unassigned

Title: NOVEL APOPTOSIS MODULATING PROTEINS, DNA ENCODING THE PROTEINS AND METHODS OF USE THEREOF

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INFORMATION DISCLOSURE

STATEMENT UNDER 37 CFR § 1.97

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

The information listed below, which may be material to the examination of the above-identified application, was previously disclosed in an Information Disclosure Statement dated April 7, 1994, directed to the parent application Serial Number 08/160,067 (filed November 30, 1993). Complete copies were also previously submitted in the parent application; therefore, copies are not included herewith. This protocol conforms with 37 CFR § 1.98(d) and MPEP 609(A)(2). The Examiner is respectfully requested to make this information of official record in the application. The information includes:

Wyllie, "Glucocorticoid-induced thymocyte apoptosis is associated with endogenous endonuclease activation" Nature (1980) 284:555-556.

Kanter et al., "Epidermal growth factor and tumor promoters prevent DNA fragmentation by different mechanisms" Biochem. Biophys. Res. Commun. (1984) 118:392-399.

Duke et al., "IL-2 addiction: Withdrawal of growth factor activates a suicide program in dependent T cells" Lymphokine Res. (1986) 5:289-299.

Tomei et al., "Inhibition of radiation-induced apoptosis *in vitro* by tumor promoters" Biochem. Biophys. Res. Commun. (1988) 155:324-331.

Kruman et al., "Apoptosis of murine BW 5147 thymoma cells induced by dexamethasone and γ-irradiation" J. Cell. Physiol. (1991) 148:267-273.

Ameisen et al., "Cell dysfunction and depletion in AIDS: The programmed cell death hypothesis" Immunol. Today (1991) 12:102-105.

Sheppard et al., "The relationship between AIDS and immunologic intolerance" J. AIDS (1992) 5:143-147.

Gerschenson et al., "Apoptosis: A different type of cell death" FASEB J. (1992) 6:2450-2455.

Cohen et al., "Apoptosis and programmed cell death in immunity" Ann. Rev. Immunol. (1992) 10:267-293.

Tsujimoto et al., "Cloning of the chromosome breakpoint of neoplastic B cells with the t(14;18) chromosome translocation" Science (1984) 226:1097-1099.

Cleary et al., "Cloning and structural analysis of cDNAs for *bcl*-2 and a hybrid *bcl*-2/immunoglobin transcript resulting from the t(14;18) translocation" Cell (1986) 47:19-28.

McDonnell et al., "Progression from lymphoid hyperplasia to high-grade malignant lymphoma in mice transgenic for the t(14;18)" Nature (1991) 349:254-256.

Edgington, "Looking death in the eye: Apoptosis and cancer research" Biotechnol. (1993) 11:787-792.

Sentman et al., "bcl-2 inhibits multiple forms of apoptosis but not negative selection in thymocytes" Cell (1991) 67:879-888.

Strasser, "*bcl*-2 transgene inhibits T cell death and perturbs thymic self-censorship" Cell (1991) 67:889-899.

Hockenbery et al., "Bcl-2 functions in an antioxidant pathway to prevent apoptosis" Cell (1993) 75:241-251.

Williams et al., "Molecular regulation of apoptosis: genetic controls on cell death" Cell (1993) 74:777-779.

Zhu et al., "Systemic gene expression after intravenous DNA delivery into adult mice" Science (1993) 261:209-211.

International (PCT) Patent Publication No. WO 93/04169 (03/04/93).

Veis et al., "Bcl-2-deficient mice demonstrate fulminant lymphoid apoptosis, polycystic kidneys, and hypopigmented hair" Cell (1993) 75:229-240.

Kiefer et al., "Molecular cloning of a new human insulin-like growth factor binding protein" Biochem. Biophys. Res. Commun. (1991) 176:219-225.

Sanger et al., "DNA sequencing with chain-terminating inhibitors" Proc. Natl. Acad. Sci. USA (1977) 74:5463-5467.

Boise et al., "*bcl*-x, a *bcl*-2-related gene that functions as a dominant regulator of apoptotic cell death" Cell (1993) 74:597-608.

Oltvai et al., "Bcl-2 heterodimerizes *in vivo* with a conserved homolog, Bax, that accelerates programed cell death" Cell (1993) 74:609-619.

Zapf et al., "Isolation from adult human serum of four insulin-like growth factor (IGF) binding proteins and molecular cloning of one of them that is increased by IGF I administration and in extrapancreatic tumor hypoglycemia" J. Biol. Chem. (1990) 265:14892-14898.

Feinberg et al., "A technique for radiolabeling DNA restriction endonuclease fragments to high specific activity" Anal. Biochem. (1984) 137:266-267.

Chen-Levy et al., "The *bcl*-2 candidate proto-oncogene product is a 24-kilodalton integral-membrane protein highly expressed in lymphoid cell lines and lymphomas carrying the t(14;18) translocation" Mol. Cell. Biol. (1989) 9:701-710.

Jacobson et al., "Bcl-2 blocks apoptosis in cells lacking mitochondrial DNA" Nature (1993) 361:365-369.

Monaghan et al., "Ultrastructural localization of BCL-2 protein" J. Histochem. Cytochem. (1992) 40:1819-1825.

Lehrach et al., "RNA molecular weight determinations by gel electrophoresis under denaturing conditions, a critical reexamination" Biochem. (1977) 16:4743-4751.

Thomas, "Hybridization of denatured RNA and small DNA fragments transferred to nitrocellulose" Proc. Natl. Acad. Sci. USA (1980) 77:5201-5205.

Barr, "Expression of foreign genes in yeast" Transgenesis (1992) Murray, J.A.H., ed., Wiley & Sons, New York, pp. 55-79.

The following information is cited on pages 22-26 of the above-identified patent application as originally filed. The Examiner is requested to note that this information was not previously disclosed in the parent application; therefore, complete copies are included herewith. The information includes:

Henderson et al., "Epstein-Barr virus-coded BHRF1 protein, a viral homologue of Bcl-2, protects human B cells from programmed cell death" Proc. Natl. Acad. Sci. USA (1993) 90:8479-8483.

Viegas-Péquignot, "*In situ* hybridization to chromosomes with biotinylated probes" *In Situ* Hybridization. A Practical Approach, D.G. Wilkinson, ed., IRL Press, Oxford, pp. 137-158.

Pinkel et al., "Fluorescence *in situ* hybrization with human chromosome-specific libraries: Detection of trisomy 21 and translocations of chromosome 4" Proc. Natl. Acad. Sci. USA (1988) 85:9138-9142.

McKearn et al., "Enrichment of hematopoietic precursor cells and cloning of multipotential B-lymphocyte precursors" Proc. Natl. Acad. Sci. USA (1985) 82:7414-7418.

Nuñez et al., "Deregulated Bcl-2 gene expression selectively prolongs survival of growth factor-deprived hemopoietic cell lines" J. Immunol. (1990) 144:3602-3610.

Hockenbery et al., "Bcl-2 is an inner mitochondrial membrane protein that blocks programmed cell death" Nature (1990) 348:334-336.

The references above are summarized throughout the application as originally filed. The summaries contain what the undersigned believes to be the salient aspects of the cited references. They are not intended to be a

comprehensive statement of the relevance of the references to the subject invention.

The following information may be material to the above-identified patent application. The Examiner is requested to note that this information was not previously disclosed in the parent application; therefore, complete copies are included herewith. The information includes:

Cherif et al., "Ordering markers in the region of the ataxia-telangiectasia gene (11q22-q23) by fluorescence *in situ* hybridization (FISH) to interphase nuclei" Hum. Genet. (1994) 93:1-6.

Foroud et al., "Localization of an ataxia-telangiectasia locus to a 3-cM interval on chromosome 11q23: Linkage analysis of III families by an international consortium" Am. J. Hum. Genet. (1991) 49:1263-1279.

Kapp et al., "Cloning of a candidate gene for ataxia-telangiectasia group D" Am. J. Hum. Genet. (1992) 51:45-54.

Khati et al., "Genetic heterogeneity of autosomal dominant cerebellar ataxia type 1: Clinical and genetic analysis of 10 French families" Neurology (1993) 43:1131-1137.

Meyn, "Ataxia-telangiectasia, apoptosis and cellular responses to DNA damage: A model" Cancer Genet. (1993) 53:(Abstract no. 1529).

Orr et al., "Expansion of an unstable trinucleotide CAG repeat in spinocerebellar ataxia type 1" Nature Genetics (1993) 4:221-226.

International (PCT) Patent Publication No. WO 94/00572 (01/06/94).

International (PCT) Patent Publication No. WO 95/00160 (01/05/95).

International (PCT) Patent Publication No. WO 95/00642 (01/05/95).

Kennedy, "Prevention of carcinogenesis by protease inhibitors" Cancer Res. (1994) 54:1999s-2005s.

Lam et al., "Evidence that BCL-2 represses apoptosis by regulating endoplasmic reticulum-associated Ca^{2+} fluxes" Proc. Natl. Acad. Sci. USA (1994) 91:6569-6573.

Reed et al., "Antisense-mediated inhibition of *BCL2* protooncogene expression and leukemic cell growth and survival: Comparisons of phosphodiester and phosphorothioate oligodeoxynucleotides" Cancer Res. (1990) 50:6565-6570.

Yonehara et al., "A cell-killing monoclonal antibody (ANTI-Fas) to a cell surface antigen co-downregulated with the receptor of tumor necrosis factor" J. Exp. Med. (1989) 169:1747-1756.

This Information Disclosure Statement is submitted before receipt of the first Office Action on the Merits. Therefore, the applicants believe that no fee is due. However, the Commissioner is hereby authorized to charge any fees which may be required by this paper to Deposit Account Number 03-1952.

Applicants would appreciate the Examiner's initialling and returning the Form PTO-1449, indicating that the references have indeed been considered and made of record herein.

This Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

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Date: March 23, 1995

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